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AGA Clinical Practice Update on the Management of Ascites, Volume Overload, and Hyponatremia in Cirrhosis: Expert Review

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DESCRIPTION: The purpose of this American Gastroenterological Association (AGA) Institute Clinical Practice Update (CPU) is to summarize the available evidence and offer expert Best Practice Advice (BPA) on the management of ascites, hepatic hydrothorax, volume overload, and hyponatremia in patients with cirrhosis. **METHODS:** This expert review was commissioned and approved by the AGA Institute Governing Board and Clinical Practice Updates Committee (CPUC) to provide timely guidance on a topic of high clinical importance to the AGA membership. This CPU expert review underwent internal peer review by the CPUC and external peer review through the standard procedures of *Gastroenterology*. These BPA statements were developed based on review of the published literature and expert opinion and approved by the AGA Institute Governing Board. Because formal systematic reviews were not performed, these BPA statements do not carry formal ratings of the quality of evidence or strength of the presented considerations.

BEST PRACTICE ADVICE STATEMENTS

BEST PRACTICE ADVICE 1: Patients with cirrhosis with ascites, hepatic hydrothorax, or volume overload should be managed with dietary sodium restriction and diuretics at the lowest effective dose, with dose escalation guided by symptoms, weight, urine output, and electrolyte/renal monitoring. Education and referral to a dietitian should be provided for dietary management. Triggers of liver decompensation should be identified and addressed. **BEST PRACTICE ADVICE 2:** Patients with cirrhosis with new-onset ascites, or those admitted to the hospital for symptoms related to ascites or encephalopathy should receive diagnostic paracentesis as soon as possible. Testing should include serum ascites albumin gradient and cell count, Gram stain, and culture. **BEST PRACTICE ADVICE 3:** Patients with hepatic hydrothorax with dyspnea and/or hypoxemia should undergo a therapeutic thoracentesis for both symptom relief and expansion of the underlying lung. **BEST PRACTICE ADVICE 4:** All patients with refractory ascites and/or hepatic hydrothorax should be considered for liver transplantation evaluation, regardless of their Model for End-Stage Liver Disease score. **BEST PRACTICE ADVICE 5:** Refractory ascites and/or hydrothorax should be managed with therapeutic paracentesis and/or thoracentesis, respectively, with the frequency guided by recurrence. **BEST PRACTICE ADVICE 6:** When the volume of ascites removed is >5 L, 20%–25% intravenous albumin 6–8 g per every total liter removed should be administered. For patients with hypotension, renal insufficiency, or electrolyte abnormalities, albumin should also be considered for removal of smaller volumes. **BEST PRACTICE ADVICE 7:** Well-selected patients with refractory ascites, hepatic hydrothorax, volume overload, or hyponatremia should be referred for to transjugular intrahepatic portosystemic shunt. **BEST PRACTICE ADVICE 8:** Diagnostic workup for the etiology of hyponatremia in cirrhosis should include dietary and medication history (diuretics, bowel regimen); review of electrolyte and kidney function; gastrointestinal bleeding assessment; infectious workup, including diagnostic paracentesis, and evaluation of secondary causes (thyroid or adrenal dysfunction). **BEST PRACTICE ADVICE 9:** Outpatient management of asymptomatic hypervolemic hyponatremia in liver cirrhosis entails both sodium and water restriction (aiming for 1–1.5 L of daily fluid intake), modification of diuretics and laxatives, and monitoring of electrolytes. **BEST PRACTICE ADVICE 10:** Inpatient management of severe or symptomatic hypervolemic hyponatremia in liver cirrhosis includes both sodium and water restriction; modification or discontinuation of diuretics and laxatives; and additional measures, such as intravenous albumin based on volume assessment or oral vasoconstriction therapy. **BEST PRACTICE ADVICE 11:** Recurrent or refractory hyponatremia management should involve a multidisciplinary approach (including the liver transplantation team when appropriate) and can consider several therapeutic options, including intravenous vasoconstrictor therapy, infusion of hypertonic saline, use of vasopressin receptor antagonist (vaptans), or use of renal replacement therapy. **BEST PRACTICE ADVICE 12:** Inpatient management of volume overload includes escalation or trial of intravenous loop diuretics (furosemide or bumetanide) in bolus (2–3 times per day) or continuous fashion. Cautious escalation can be done every 2–3 days with monitoring of volume status, kidney function, daily weights, and symptoms. **BEST PRACTICE ADVICE 13:** Advanced strategies in refractory anasarca should be coordinated with nephrology for consideration of diuretics in the setting of contraction alkalosis (eg, addition of acetazolamide), second agent with alternate mechanism of actions (eg, thiazide diuretics, such as metolazone), or need for ultrafiltration.

Keywords: Diuretics; Hepatic Hydrothorax; Liver Transplantation; Paracentesis; Transjugular Intrahepatic Portosystemic Shunt; Peritonitis Diagnosis; Peritonitis Treatment; Hyponatremia; Hepatorenal Syndrome; Thoracentesis; Practice Guidance; Review.

Volume overload is a defining feature of decompensated cirrhosis and can manifest as ascites, hepatic hydrothorax (HH), peripheral edema, and anasarca. It

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Abbreviations used in this paper: **HE, hepatic encephalopathy; HH, hepatic hydrothorax; MELD, Model for End-Stage Liver Disease; SAAG, serum ascites albumin gradient; SBE, spontaneous bacterial empyema; SBP, spontaneous bacterial peritonitis; TIPS, transjugular intrahepatic portosystemic shunt.**

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results from portal hypertension, where increased intrahepatic vascular resistance and portal blood flow trigger mesenteric and systemic vasodilation. The kidney responds with neurohormonal activation of the renin-angiotensin-aldosterone system promoting renal sodium and water reabsorption, leading to expansion and redistribution of intravascular and interstitial volume.[1,2] Excess fluid then leaks directly into the peritoneal cavity, causing ascites as a result of exceeding the capacity of the hepatic lymphatic system, while in a state of reduced oncotic pressure (hypoalbuminemia), increased hydrostatic pressure (portal hypertension), and increased capillary permeability. Ascites is not the only manifestation of cirrhosis-related volume overload; diaphragmatic defects allow fluid to enter the pleural space, causing HH. Excess fluid can also accumulate in interstitial spaces, leading to peripheral edema and anasarca. With progressive circulatory dysfunction and effective intravascular hypovolemia, renal water retention increases, resulting in hypervolemic hyponatremia.[3]

These complications of portal hypertension impact patients through decreased quality of life and repeated hospitalizations.[4–8] Volume overload predisposes to infections, hepatorenal syndrome, and increased mortality.[9–11] Hyponatremia worsens hepatic encephalopathy (HE) and ascites and is associated with mortality.[12,13]

Managing volume overload is complex. Treatment may cause renal insufficiency and electrolyte imbalances, requiring close monitoring and frequent medication adjustments. Advanced therapies require experienced multidisciplinary teams (eg, transjugular intrahepatic portosystemic shunt [TIPS], liver transplantation). This review offers best practice advice on diagnosing and managing ascites, volume overload, and hyponatremia in cirrhosis.

Best Practice Advice 1: Patients with cirrhosis with ascites, HH, or volume overload should be managed with dietary sodium restriction and diuretics at the lowest effective dose, with dose escalation guided by symptoms, weight, urine output, and electrolyte/renal monitoring. Education and referral to a dietitian should be provided for dietary management. Triggers of liver decompensation should be identified and addressed.

The natural history of cirrhosis involves progression through stages marked by decompensating events (ascites, HE, variceal bleeding). Decompensation reduces survival from >12 years to approximately 2 years.[14] Ascites is the most common initial event. Identifying and addressing triggers, such as alcohol, medications, toxins, hemodynamic changes (eg, shock, surgery), or infection, is critical. For example, blood pressure–lowering medications, especially inhibitors of the renin-angiotensin system, may need to be held. Management targets underlying sodium avidity, requiring a negative sodium balance via dietary restriction and diuretics (Figure 1).

Referral to a dietitian should be made to support sodium restriction, ideally to <2000 mg/d. A dietitian can guide patients and caregivers in label reading, cooking techniques, and sodium education. The US Food and Drug Administration provides a helpful online educational resource (https://www.fda.gov/food/nutrition-education-resources-materials/sodium-your-diet), and the sodium contents of common foods are listed in Supplementary Table 1. Diets must not become overly restrictive, risking caloric or protein deficiency in these often-malnourished patients. Dietary advice includes ≥35 kcal/kg/d (non-obese), micronutrient repletion, and protein intake of 1.2–1.5 g/kg.[15] Fluid restriction is not needed in the absence of significant hyponatremia.

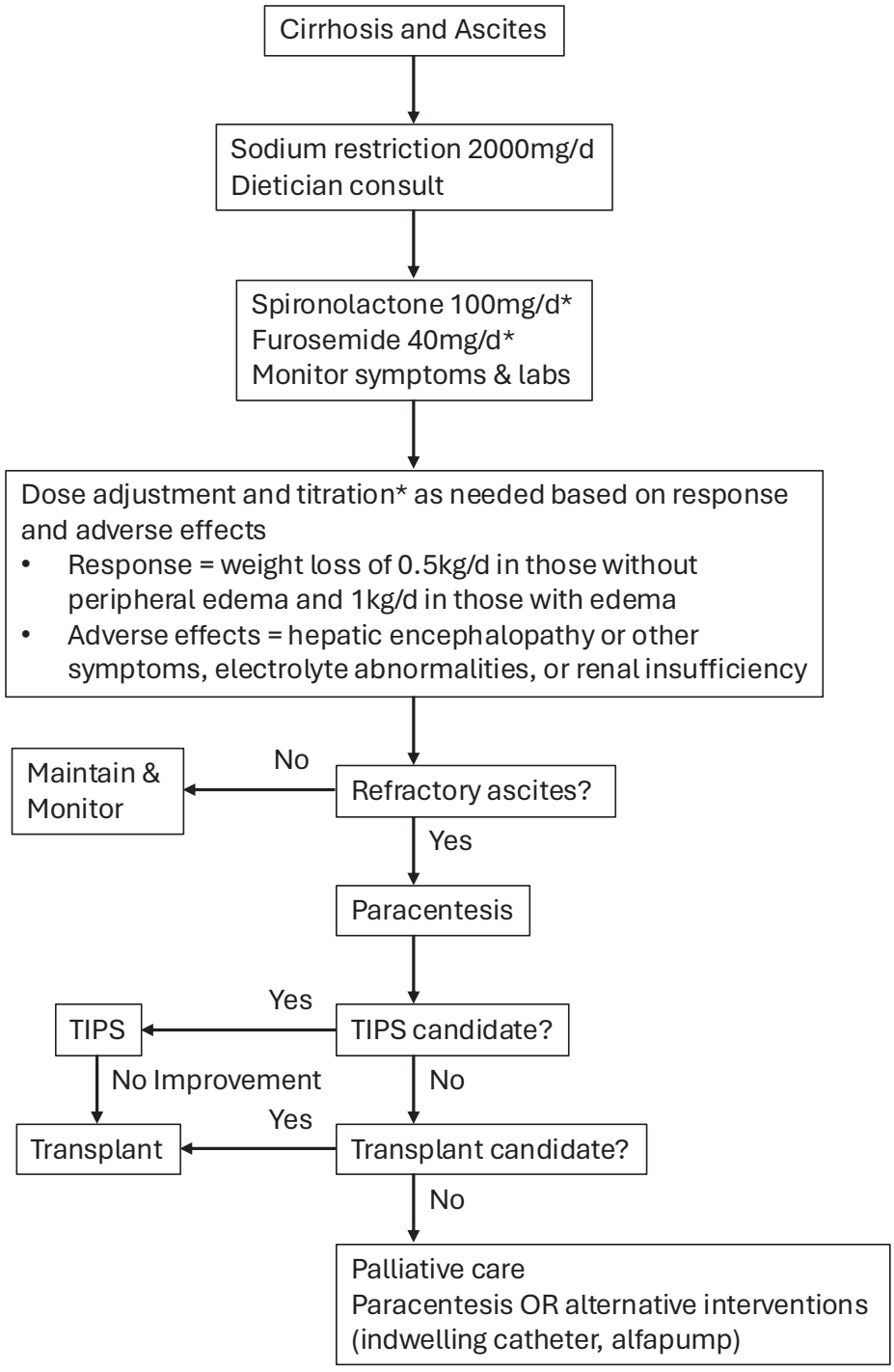
Mineralocorticoid receptor antagonists and loop diuretics are first-line medications for ascites and work by inducing natriuresis. Combined furosemide and spironolactone (40:100 ratio) enhance natriuresis and diuresis while maintaining normokalemia, outperforming mineralocorticoid receptor antagonist monotherapy or sequential use.[16] Spironolactone is typically started at 100 mg daily (range, 50–400 mg), ideally as a once-daily morning dose due to its long half-life and to avoid nocturia with evening dosing.[17,18] Alternatives (eg, amiloride, eplerenone) are options for spironolactone-intolerant patients, although they are less effective.

Furosemide usually starts at 40 mg daily (range, 20–160 mg), with dosing guided by ascites severity, blood pressure, electrolytes, and renal function. Diuretics should be titrated to the lowest effective dose based on weight, symptoms, urine output, and laboratory test results. Patients should weigh themselves daily, with targeted weight loss of 0.5 kg/d without edema (1 kg/d with edema). Mild, asymptomatic ascites may be managed with low-dose diuretics or sodium restriction alone.

Best Practice Advice 2: Patients with cirrhosis with new-onset ascites, or those admitted to the hospital for symptoms related to ascites or encephalopathy should receive a diagnostic paracentesis as soon as possible. Testing should include serum ascites albumin gradient (SAAG) and cell count, Gram stain, and culture.

Although cirrhosis accounts for >85% of ascites in the West, other causes (eg, heart failure) should be excluded. A diagnostic paracentesis is necessary, with calculation of the SAAG by subtracting ascites albumin from serum albumin. Testing for SAAG may be appropriate when there is concern for non–cirrhosis-related ascites and cell count is a key test for asymptomatic/unsuspected spontaneous bacterial peritonitis (SBP). SAAG ≥1.1 g/dL strongly suggests portal hypertension, whereas SAAG <1.1 g/dL warrants evaluation for other causes. Patients with heart failure typically have SAAG ≥1.1 g/dL and high ascitic fluid protein (>2.5 g/dL).

Paracentesis is indicated for all hospitalized patients with cirrhosis with ascites due to the high risk of SBP, even without signs of infection. Paracentesis within 12–24 hours of admission is associated with lower hospital mortality.[19,20] Ascites should be analyzed for cell count, Gram stain, and cultures. SBP is diagnosed when the neutrophil count exceeds 250/mm^3, with or without culture positivity, and without evidence of secondary peritonitis. Cultures should be obtained by bedside inoculation into blood culture bottles. Ascites with low SAAG or features suggesting non–portal hypertension causes should undergo further



*Suggested doses 50-400mg/d for spironolactone and 20-160mg/d for furosemide

Figure 1. Management of ascites in patients with cirrhosis.

testing, such as cytology, amylase, and mycobacterial studies.

Best Practice Advice 3: Patients with HH with dyspnea and/or hypoxemia should undergo a therapeutic thoracentesis for both symptom relief and expansion of the underlying lung.

HH is a pleural effusion occurring in the setting of portal hypertension without other causes (eg, heart failure, lung disease, malignancy). It results from translocation of ascitic fluid through diaphragmatic pores and is a poor prognostic sign, associated with a >4-fold increase in mortality compared with refractory ascites.[21]

A diagnostic thoracentesis helps exclude other causes of pleural effusion. Hospitalized patients with HH-related symptoms, HE, or unexplained liver decompensation should undergo thoracentesis to evaluate for spontaneous bacterial empyema (SBE). Thoracentesis is indicated for all hospitalized patients with cirrhosis with new-onset HH due to the high risk of SBE even without signs of infection. Like SBP, SBE is diagnosed when pleural fluid neutrophils exceed 250/mm^3, with or without culture positivity, and without an alternative infectious source.

Compared with ascites, HH causes symptoms at much lower fluid volumes. Sodium restriction and diuretics are first-line therapies. Symptomatic patients or those with recurrent effusions despite treatment should undergo therapeutic thoracentesis.

Best Practice Advice 4: All patients with ascites and/or HH should be considered for liver transplantation evaluation, regardless of their Model for End-Stage Liver Disease (MELD) score.

Ascites is the most common form of cirrhosis decompensation and marks a critical step in the disease's natural history. It is a prerequisite for SBP and hepatorenal syndrome, which carry 90-day mortality rates up to 50%.[10,22] Ascites is also linked to malnutrition, sarcopenia, and frailty—factors that increase mortality and may preclude transplantation.[23–26] Once ascites develops, annual mortality rises from <5% to 20%.[14] Given these poor outcomes, all patients with cirrhosis and ascites should be considered for transplantation, regardless of MELD score. MELD has been revised to best reflect waitlist mortality and reduce transplantation disparities by including sodium, sex, and albumin.[13,27] Despite these changes, ascites remains an independent predictor of mortality beyond MELD.[11,28] Patients with ascites and low MELD scores may access transplants via living donors or extended criteria donors.

Compared with ascites, HH is independently associated with significantly higher mortality regardless of MELD, with 1-year mortality rate of 20%–50%.[21,29] Currently, Organ Procurement and Transplantation Network guidance offers no standard MELD exception for HH, although nonstandard exceptions may be granted individually for patients meeting criteria: ≥1 thoracentesis >1 L weekly for 4 weeks, transudative fluid, no heart failure, negative cultures and cytology, and contraindications to TIPS.[30]

Best Practice Advice 5: Refractory ascites and/or hydrothorax should be managed with therapeutic paracentesis and/or thoracentesis, respectively, with the frequency guided by recurrence.

Refractory ascites is defined as "ascites that cannot be mobilized or the early recurrence of which cannot be satisfactorily prevented by medical therapy"[31] (Table 1). It is subcategorized as diuretic-resistant (ie, nonresponse to sodium restriction and diuretics) or diuretic-intractable (ie, complications that prevent effective diuretic dose escalation).[32] Refractory HH is similarly defined as unresponsive to sodium restriction and diuretics.

Therapeutic paracentesis is a safe, effective method for ascites management.[33,34] Compared with intensive diuretic therapy, paracentesis offers faster symptom relief and fewer complications (eg, HE, electrolyte abnormalities, and acute kidney injury). Large-volume removal can cause postparacentesis circulatory dysfunction, marked by reduced systemic vascular resistance and activation of the renin-angiotensin and sympathetic systems.[35] This raises the risks of kidney injury, electrolyte imbalances, HE, and death—although these risks may be mitigated by judicious albumin infusion.[36,37] Postparacentesis bleeding is rare, even with coagulopathy or thrombocytopenia; prophylactic transfusions are not advised.[38–40]

Compared with refractory ascites, refractory HH is more challenging due to lower fluid thresholds for symptoms and differing presentations (dyspnea vs distention). Thoracentesis is generally safe, but carries higher risks (eg, bleeding, infection, pneumothorax, and re-expansion edema) in HH than in other effusion causes.[41] Although rare, bleeding from chest wall portosystemic collaterals can be catastrophic. Risks of complications and death rise with repeated thoracenteses.[21,41]

Chest tube placement for HH carries high morbidity and mortality and should be avoided.[42] Conversely, indwelling tunneled pleural catheters have shown promise, with relatively low complication rates.[43,44] These may serve as palliative options for non–transplantation candidates or as a bridge to transplantation with short wait times.

Table 1. Definitions of Volume Overload-Related Conditions Cirrhosis

Term	Definition
Refractory ascites	Ascites that cannot be mobilized or the early recurrence of which cannot be satisfactorily prevented by medical therapy
Refractory HH	HH that is unresponsive to salt restriction and diuretic therapy and requires therapeutic thoracentesis
Refractory hyponatremia	Ongoing hyponatremia despite maximal medical therapy
Refractory anasarca	Lack of improvement in volume status despite maximal diuretics and persistent low urine sodium

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Best Practice Advice 6: When the volume of ascites removed is >5 L, 20%–25% intravenous albumin 6–8 g per every total liter removed should be administered. For patients with hypotension, renal insufficiency, or electrolyte abnormalities, albumin should also be considered for removal of smaller volumes.

Postparacentesis circulatory dysfunction is a well-characterized complication of large volume paracentesis associated with poor outcomes. To prevent this, it is standard to administer 20%–25% intravenous albumin after paracentesis >5 L, which reduces electrolyte derangements and mortality.[45] The 5 L cutoff and 6–8 g/L albumin dose are somewhat arbitrary. Recent data suggest smaller-volume paracentesis may also benefit from albumin; however, additional dose-defining studies are needed, as different albumin doses have not shown differences in outcomes.[46,47]

Profound portal hypertension in refractory ascites often coexists with hypotension, renal insufficiency, and electrolyte abnormalities. These conditions pose additional clinical challenges, as rapid volume shifts may have amplified effects and postparacentesis circulatory dysfunction consequences may be more severe.[37] In this population, a more liberal albumin strategy using lower-volume thresholds and higher doses may be considered case by case, with care to avoid iatrogenic volume overload.

Best Practice Advice 7: Well-selected patients with refractory ascites, hepatic hydrothorax, volume overload, or hyponatremia should be referred for TIPS.

TIPS is a highly effective treatment for portal hypertension, used for ascites, HH, or variceal bleeding.[48] It is more effective than paracentesis in controlling ascites and is associated with lower mortality.[49,50] However, its impact on patient-reported outcomes is less clear. Symptom relief may be offset by HE and TIPS dysfunction risk.[51] Contemporary use of polytetrafluoroethylene-covered stents may reduce these risks, although supporting data are limited.[50,52,53]

Patient selection for TIPS is critical. Absolute contraindications include congestive heart failure, severe pulmonary hypertension, uncontrolled HE, and sepsis.[48] TIPS should be avoided in patients with ejection fraction <50%, severe diastolic/valvular dysfunction, or right ventricular systolic pressure >45 mm Hg.[54] HE occurs in up to 50% post-TIPS.[55] Risk factors include prior HE, impaired liver function, older age, renal dysfunction, hyponatremia, large gradient reduction, and sarcopenia.[53] Caution is advised for patients older than 70 years or with MELD score >18, although increasingly the indication is being expanded in this population.[56,57] Cardiac decompensation may occur in up to 20% within 1 year of TIPS.[54] Preprocedural evaluation of cardiac systolic/diastolic function and right ventricular systolic pressure via echocardiography should be performed.

Optimal TIPS timing remains undefined. Most studies focus on refractory ascites and HH.[48] One study in patients with <6 paracenteses in 3 months showed better ascites control, fewer hospitalizations, and improved survival without more HE.[50] This early TIPS strategy may be cost-effective but needs validation.[58] Some expert panels suggest TIPS after 3 large-volume paracenteses in 12 months, especially in those with other indications (eg, prior variceal bleeding episode), but data are limited and more studies are needed.[54,59]

For refractory ascites patients not eligible for TIPS, limited evidence supports indwelling peritoneal catheters.[60,61] However, complication rates may be high. The alfapump (Sequana Medical), which transfers ascites into the bladder, has improved quality of life in randomized trials, but carries risk of infection.[62,63] It was recently approved in the United States, but widespread experience is lacking. For select non–TIPS candidates, peritoneovenous shunt placement may be considered, although it is limited by concerns regarding shunt patency, disseminated intravascular coagulation, and heart failure.[64]

Best Practice Advice 8: Diagnostic workup for the etiology of hyponatremia in cirrhosis should include dietary and medication history (diuretics, bowel regimen); review of electrolyte and kidney function; gastrointestinal bleeding assessment; infectious workup, including diagnostic paracentesis; and evaluation of secondary causes (thyroid or adrenal dysfunction).

Among patients with cirrhosis and ascites, hyponatremia—defined as serum sodium <130 mEq/L—is due to serum overdilution from fluid retention caused by vasopressin secretion, increased water reabsorption and subsequent enhanced sodium reabsorption.[32,65,66] This hypervolemic hyponatremia is associated with significant morbidity and mortality.[13] Due to these adverse outcomes, serum sodium was incorporated into the transplant allocation system within MELD.[67] However, when hyponatremia occurs in a patient with cirrhosis, other etiologies must be considered. Daily documentation of sodium and fluid intake, alcohol use, medications (eg, diuretics and laxatives), and assessment of renal, thyroid, adrenal, and cardiac function is imperative.[68] Hyponatremia may also signal acute inflammation; it is essential to evaluate for infection with cultures, including diagnostic paracentesis.[69] Pseudohyponatremia is a laboratory artifact often seen in the presence of hypertriglyceridemia or paraproteinemia, that should be considered if the serum osmolality is not low (>280 mOsm/L). If nonhepatic causes are identified, targeted management should follow.

Best Practice Advice 9: Outpatient management of asymptomatic hypervolemic hyponatremia in liver cirrhosis entails both sodium and water restriction (aiming for 1–1.5 L of daily fluid intake), modification of diuretics and laxatives, and monitoring of electrolytes.

Management of hypervolemic hyponatremia in cirrhosis begins with dietary sodium and fluid restriction based on severity (Figure 2). If asymptomatic with mild hyponatremia (serum sodium >120 mEq/L), management can include limiting fluid intake to 1–1.5 L.[32,67,68] Diuretics often need to be reduced or discontinued. Once sodium stabilizes >125 mEq/L, providers can resume or maintain diuretics. Patient education on lactulose (and other laxative) dosing is important to avoid excessive stooling, which

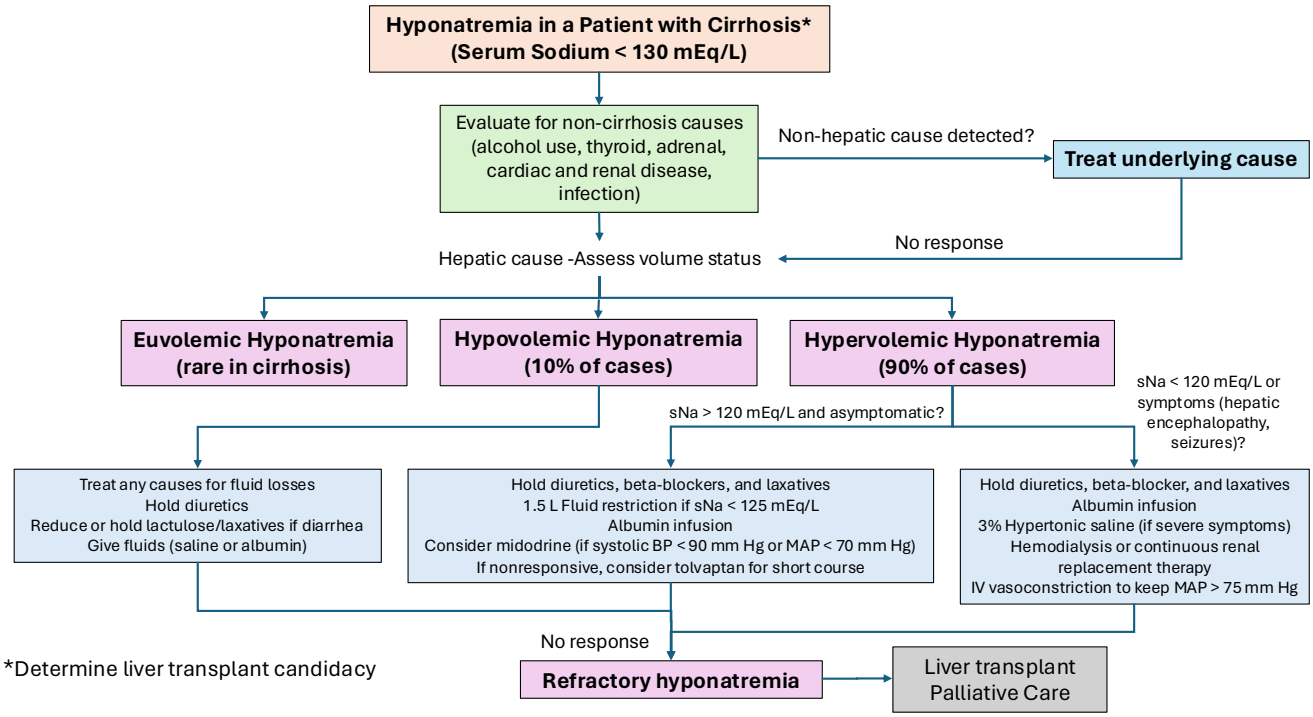
Hyponatremia in a Patient with Cirrhosis*
(Serum Sodium < 130 mEq/L)
Evaluate for non-cirrhosis causes
(alcohol use, thyroid, adrenal,
cardiac and renal disease,
infection)
Non-hepatic cause detected?
Treat underlying cause
No response
Hepatic cause -Assess volume status
Euvolemic Hyponatremia
(rare in cirrhosis)
Hypovolemic Hyponatremia
(10% of cases)
Hypervolemic Hyponatremia
(90% of cases)
sNa < 120 mEq/L or
symptoms (hepatic
encephalopathy,
seizures)?
sNa > 120 mEq/L and asymptomatic?
Treat any causes for fluid losses
Hold diuretics
Reduce or hold lactulose/laxatives if diarrhea
Give fluids (saline or albumin)
Hold diuretics, beta-blockers, and laxatives
1.5 L Fluid restriction if sNa < 125 mEq/L
Albumin infusion
Consider midodrine (if systolic BP < 90 mm Hg or MAP < 70 mm Hg)
If nonresponsive, consider tolvaptan for short course
Hold diuretics, beta-blocker, and laxatives
Albumin infusion
3% Hypertonic saline (if severe symptoms)
Hemodialysis or continuous renal
replacement therapy
IV vasoconstriction to keep MAP > 75 mm Hg
No response
*Determine liver transplant candidacy
Refractory hyponatremia
Liver transplant
Palliative Care

Figure 2. Algorithm for the management of hyponatremia in cirrhosis.

can lead to volume depletion and worsening hyponatremia. Serial electrolyte and renal function monitoring is critical. Although data are sparse, ambulatory albumin infusions may help hyponatremia, but access is limited by insurance and infusion site availability.[70–72]

Best Practice Advice 10: Inpatient management of severe or symptomatic hypervolemic hyponatremia in liver cirrhosis includes both sodium and water restriction; modification or discontinuation of diuretics and laxatives; and additional measures, such as intravenous albumin based on volume assessment or oral vasoconstriction therapy.

When patients develop symptoms related to hyponatremia or serum sodium falls below 120 mEq/L, hospitalization should be strongly considered. Symptoms can include cognitive changes, dizziness, seizures, cardiopulmonary alterations, nausea, and vomiting.[73,74] Patients should be evaluated for precipitants, including infections. Diuretics and laxatives should be discontinued or adjusted, and renal and cardiac function assessed. Hypokalemia should be corrected especially in the presence of encephalopathy. Fluid intake should be restricted to be less than urine output. In hypotension (systolic blood pressure <90 mm Hg), nonselective beta-blockers for portal hypertension may need to be held, and endoscopic management of high-risk varices pursued for those unable to resume beta-blockers.[75] In severe symptomatic cases, immediate interventions, such as albumin infusion or vasoconstrictors (eg, midodrine) can improve renal perfusion.[70,71,76] Life-threatening hyponatremia or cases requiring correction before liver transplantation may warrant cautious 3% hypertonic saline use, avoiding rapid correction to prevent osmotic demyelination syndrome.[77] Selective vasopressin antagonists (ie, vaptans) can improve hyponatremia in cirrhosis; however, their use has declined due to adverse events, including hepatic injury and mortality.[78–81] Vaptans are now reserved mainly for short-term use in patients with severe hyponatremia awaiting liver transplantation. In severe kidney injury, hemodialysis may also help correct hyponatremia.[82]

Best Practice Advice 11: Recurrent or refractory hyponatremia management should involve a multidisciplinary approach (including the liver transplantation team when appropriate) and can consider several therapeutic options, including intravenous vasoconstrictor therapy, infusion of hypertonic saline, use of vasopressin receptor antagonist (vaptans), or use of renal replacement therapy.

Recurrent or refractory hyponatremia in cirrhosis, like ascites, reflects a progressive hemodynamic insult amid severe fluid retention. Hyponatremia recurs in >50% of cases and is associated with poor survival.[83] Like ascites, redevelopment after a prior episode or persistence despite maximal therapy defines recurrent and refractory hyponatremia, respectively. Ongoing hyponatremia carries significant short-term mortality and, as severity increases, so does the need for liver transplantation.[13] Management requires a multidisciplinary approach, including transplant hepatology, nephrology, and potentially anesthesiology. While evaluating other causes (eg, adrenal insufficiency), vasoconstrictor therapy (eg terlipressin or norepinephrine) may improve sodium levels before transplantation.[84] Hypertonic saline can also be used for symptomatic or severe hyponatremia. Team-based decisions can guide use of

vaptans or renal replacement therapy. If transplantation is not an option, palliative care and hepatology teams can help address goals of care and symptom management.

Best Practice Advice 12: Inpatient management of volume overload includes escalation or trial of intravenous loop diuretics (furosemide or bumetanide) in bolus (2–3 times per day) or continuous fashion. Cautious escalation can be done every 2–3 days with monitoring of volume status, kidney function, daily weights, and symptoms.

The presence of anasarca with or without ascites or HH is a common presentation of cirrhosis decompensation in the inpatient setting. Inpatient management is often required in patients who progress despite outpatient diuretic dose escalation and/or have persistent signs of anasarca or volume overload. Focused study of anasarca management in cirrhosis is limited; guidance is often extrapolated from cardiology and nephrology literature.[85,86] First steps typically include reversal of aggravating factors (eg, alcohol, nonsteroidal anti-inflammatory drugs); dietary sodium restriction; medication review, including anti-hypertensives (especially renin-angiotensin system inhibitors); and diuresis. The goal is to promote urinary sodium excretion in excess of dietary sodium intake. Initial regimens include intravenous loop diuretics (furosemide or bumetanide) given in bolus (2–3 times daily) or continuous fashion. Response is gauged by daily symptom assessment, urine output, kidney function, and weights. If inadequate diuresis occurs, escalating doses in bolus or continuous fashion is pursued every 2–3 days, with monitoring of volume status, renal function, daily weights, and symptoms. Superiority of bolus vs continuous infusion remains unclear in cirrhosis.[86] Furosemide and bumetanide likely offer similar efficacy as first-line agents.[87] Torsemide may also play a role in the inpatient and outpatient setting, although it is only available orally in the United States.[88–90] Intravenous furosemide is approximately twice as potent as oral, whereas bumetanide may have 1:1 oral-to-intravenous equivalence.[91] The role of concurrent intravenous albumin is unclear.[92,93] In patients not admitted specifically for volume overload, targeting a serum albumin level does not reduce infection, kidney dysfunction, or death.[94]

Best Practice Advice 13: Advanced strategies in refractory anasarca should be coordinated with nephrology for consideration of diuretics in the setting of contraction alkalosis (eg, addition of acetazolamide), second agent with alternate mechanism of actions (eg, thiazide diuretics, such as metolazone), or need for ultrafiltration.

For patients with an inadequate response, dose escalation should be coordinated with nephrology. In refractory edema unresponsive to loop diuretics, thiazide diuretics (eg, metolazone) may be considered. Adverse events that may limit diuresis include contraction alkalosis and electrolyte dysfunction. Elevation in serum creatinine is common but may not necessarily reflect worsening kidney function.[95] In diuretic-resistant anasarca (no improvement despite maximal diuretics and persistently low urine sodium), advanced strategies include pressors to augment diuresis in the intensive care unit. Ultrafiltration may also be considered in select cases, especially for liver transplantation candidates. On discharge, transitional care with proper medication management, patient and caregiver education, and timely follow-up is important to improve outcomes in cirrhosis.[96–98]

Conclusions and Future Directions

Liver transplantation remains the only curative option for patients with cirrhosis with ascites, fluid overload, and hyponatremia. However, given the significant gap between donor organ supply and transplant demand, other strategies are needed to either bridge patients to transplantation or provide improvement in quality of life for those without timely access. There are clear needs to improve management of ascites, fluid overload, and hyponatremia in cirrhosis, and ongoing studies are warranted. Investigational therapeutic trials are especially needed for those with advanced steatotic liver disease, who carry significant comorbidities and confound older treatment paradigms on which many societal guidelines are based.

Further refinement of disease definitions is needed to enhance provider understanding and enable earlier recognition and implementation of appropriate management. Although many patients with complex fluid retention, ascites, and hyponatremia will be managed at tertiary or transplantation centers, gastroenterologists and hospitalists must know when and how to provide optimal care and timely hepatology referral. Without this successful linkage, patients may fail to connect with liver centers and face higher mortality, readmissions, and poor outcomes.[99] To complement advances in treating underlying liver disease (eg, metabolic dysfunction–associated steatotic liver disease), we must develop improved strategies for fluid overload to enhance survival, quality of life, and hope for patients and caregivers.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at https://doi.org/10.1053/j.gastro.2025.08.029.

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Conflicts of interest
These authors disclose the following: Eric S. Orman has consulted for Biovie and Sitero. Brett E. Fortune has consulted for WL Gore and Associates, BD Medical, Madrigal, Cook Medical, and Gilead Sciences. Binu V. John has reported no conflicts of interest related to this article. He has consulted for Exelixis and received institutional research support from Exact Sciences, Takeda, Genentech, and Glycotest Inc. The remaining author discloses no conflicts.

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